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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/511,824	02/24/2000	Yasuo Yamao	FUJ2-AZ72a	5341

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SNELL & WILMER LLP
1920 MAIN STREET
SUITE 1200
IRVINE, CA 92614-7230

EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 03/09/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/511,824	YAMAO ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2002 and 15 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9,11-15 and 19-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,11-15, and 19- 23* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's election of Group 1, claims 9, 11-15, and 19-23 is acknowledged and has been entered. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Non-elected claims 16-18 have been cancelled. Accordingly, claims 9, 11-15, and 19-23 are pending and are under examination.

Claim Objections

2. Claims 11 and 22 are objected to, for depending from cancelled claims, i.e. claim 8 and claim 10.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 9, 11-15, 19-21, and 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is vague and indefinite because it fails to clearly define the structural and functional cooperative relationship between the latex reagent, the agglutination reaction, and the insoluble carrier having an antibody immobilized thereto.

Claim 9 lacks clear antecedent support in reciting, "the reaction products". Additionally, it is unclear what is encompassed by the recitation of "reaction products" and what structural and functional cooperative relationship exists between the "reaction mixture" and the "reaction products" as recited in the claim.

Claim 11 is indefinite in relation to claim 9 from which it depends because it is unclear as to whether "saponin aqueous solution" is the "hemolysis reagent" recited in claim 9.

Claim 12 is vague and indefinite in relation to claim 9 from which it depends in reciting, "the measuring step is performed with the use of an erythrocyte counter" because in claim 9, the erythrocytes were caused to be hemolyzed. Thus, since an erythrocyte counter is an apparatus used in counting individual unlysed erythrocytic cells, it is unclear 1) what erythrocytes Applicant intends to count and 2) how irradiation and measurement of reaction products in a wavelength range which is substantially free from absorption by both hemoglobin and hemolysis reagent is effected using the erythrocyte counter. Accordingly, it is unclear what structural and functional cooperative relationship exists between the erythrocyte counter in the instant claim and the components of the reaction products that are intended to be irradiated and measured in claim 9.

Claim 13 is vague and indefinite because it fails to clearly define the structural and functional cooperative relationship between the latex reagent, the agglutination reaction, and the insoluble carrier having an antibody immobilized thereto.

Claim 14 is indefinite in reciting, "CRP". Acronyms or abbreviations must be fully defined and recited at least one time in a set of claims.

Claim 14 is vague and indefinite in reciting, "including the step of determining the CRP component" in plasma" because it is unclear what structural and functional cooperative relationship exists between the "CRP component" and the "predetermined antigen" that is being measured in claim 13.

Claim 19 is redundant and confusing in reciting, "adding a latex reagent to the hemolyzed whole blood" and "providing an agglutination reaction with the hemolyzed whole blood sample to form an agglutinaltion reaction product" because it would seem that upon addition of the latex reagent to the hemolyzed sample, the latex reagent having antibody immobilized onto a carrier and corresponding antigens present in the hemolyzed sample, would have undergone an agglutination reaction to form the reaction mixture. Does Applicant intend that an additional step of "further reacting" should be effected such as perhaps by addition of an activation agent into the sample. Please clarify.

Claim 19 is vague and indefinite because it fails to clearly define the structural and functional cooperative relationship between the latex reagent, the agglutination reaction product, and the insoluble carrier having an antibody immobilized thereto.

Claim 21 is indefinite in reciting, "CRP". Acronyms or abbreviations must be fully defined and recited at least one time in a set of claims.

Claim 21 is vague and indefinite because it is unclear how "CRP" is differentially detected and measured from the recited "antigens" in claim 19, to thus determine a value of CRP in the hemolyzed whole blood sample.

Claim 22 is indefinite in depending from cancelled claim 8 and lacks antecedent support in reciting, "the means for measuring".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 9, 11, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bradwell et al. (US Patent 4,889,815) in view of Loretz (US Patent 4,357,105).

Bradwell et al. disclose an agglutination assay wherein a whole blood sample is lyzed with a hemolysis reagent (saponin/KCN) then reacted with a latex reagent comprising insoluble carriers with antibodies immobilized thereto (latex bound antibodies) to react with antigens in the whole blood sample to thus, form a reaction mixture (see column 3, lines 16-33). Bradwell et al. teach using a nephelometer in analyzing the reaction mixture without the need to remove blood cells or hemoglobin (see column 1, lines 51-54). A second detector is included to compensate for the amount of light absorbed possibly by the hemoglobin in the sample to minimize and correct for any degree of absorption by the hemoglobin in the sample (see column 1, lines 21-25, 51-54; column 3, lines 16-54 ; column 4, lines 59-61). In the system, wavelength is read where the strength of radiation scattered by antigen/antibody complex is high and the absorption by hemoglobin and other proteins is low.

Bradwell et al. differ in failing to irradiate and measure the reaction product at a wavelength range that is substantially free from absorption by both hemoglobin and hemolysis reagent.

Loretz discloses using a blood diagnostic spectrophotometer to perform hemoglobin determinations in blood. The spectrophotometer is capable of measuring turbidity in blood (see Abstract). Loretz uses saponin to hemolyze the whole blood (see column 2, lines 47-66). According to Loretz, blood turbidity can be determined by measuring at a wavelength that is near- infrared. Specifically, Loretz discloses that

absorbance measurements of blood lipid levels at or near infra-red range are substantially free from the absorbance of hemoglobin (see column 7).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to irradiate and measure the reaction product in the method of Bradwell, at a wavelength range that is free from absorption and interference by hemoglobin as taught in the method of Loretz, because Bradwell specifically suggested determining analyte concentration at a wavelength range having minimal effect by hemoglobin and also correcting for any degree of absorption by hemoglobin in the sample to thus, remove any interfering effect by hemoglobin, and Loretz specifically showed that absorbance at a wavelength range substantially free from effects of hemoglobin can be achieved, at or near infrared wavelength. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the teaching of Loretz in wavelength ranges substantially free from the effects of hemoglobin, into the method of determining analyte concentration at wavelength range having minimal effect by hemoglobin because by providing a wavelength that totally eliminates unwanted absorbance from interfering substances, such as in this case, hemoglobin, accuracy in assay methods can be better achieved.

5. Claims 9, 11, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bradwell et al. (US Patent 4,889,815) in view of Osten et al. (US Patent 5,729,333).

Bradwell et al. has been discussed supra. Bradwell et al. differ in failing to irradiate and measure the reaction product at a wavelength range that is substantially free from absorption by both hemoglobin and hemolysis reagent.

Osten et al. provide a method for characterizing properties of biological matter containing water by analyzing at near-infrared spectrum of the biological matter while in a dynamic condition. Osten et al. specifically disclose that absorbance of water in the 1150-1190 nm range is substantially free from the absorbance of hemoglobin both in its oxygenated state and deoxygenated state (see columns 3-4, especially column 4, lines 42-58).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to irradiate and measure the reaction product in the method of Bradwell, at a wavelength range that is free from absorption by hemoglobin as taught in the method of Osten, because Bradwell specifically suggested determining analyte concentration at a wavelength range having minimal effect by hemoglobin and also correcting for any degree of absorption by hemoglobin in the sample, and Osten specifically showed that absorbance at a wavelength range substantially free from effects of hemoglobin can be achieved, i.e. 1150-1190 in the case of biological matter containing water. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the teaching of Osten in 1150-1190 nm wavelength range which is substantially free from the effects of hemoglobin, into the method of determining analyte concentration at wavelength range having minimal effect by hemoglobin because by providing a wavelength that totally eliminates unwanted

absorbance from interfering substances, such as in this case, hemoglobin, accuracy in assay methods can be better achieved.

6. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bradwell et al. (US Patent 4,889,815) in view of Loretz (US Patent 4,357,105) or Osten et al. (US Patent 5,729,333) as applied to claim 13 above, and further in view of Schoessler et al. (Development and Application of Latex-agglutination assay for the determination of C-Reactive Protein).

Bradwell et al., Loretz, and Osten et al. have been discussed supra. Bradwell et al., Loretz, and Osten et al. differ from the instant invention in failing to disclose determining CRP in plasma in the hemolyzed blood sample.

Schoessler et al. teach using latex-agglutination assay for detection of C-reactive protein (CRP). The assay principle is based on adsorptive linkage or immobilization of anti-CRP antibodies to latex particles.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to quantitate CRP as taught by Schoessler by irradiating and measuring agglutination assay products at a wavelength range that is free from absorption by hemoglobin, as suggested by Bradwell as modified by Loretz or Osten because CRP constitutes an obvious variation of detectable analytes which are routinely varied in the immunological art and all of Bradwell, Loretz, and Osten are generic with respect to the types of analytes that to be assayed.

Response to Arguments

7. Applicant's arguments filed 10/30/02 and 12/15/03 have been fully considered but they are not persuasive.

A) Applicant argues that the combination of Bradwell with Loretz does not render obvious the claimed invention. Applicant specifically contends that Bradwell only discloses a wavelength range approximately 400 to 600 nm and thus, discloses an on-axis detector that is used to time the duration of light flash to particularly compensate for absorption of hemoglobin. Applicant also argues that the Office has ignored the teaching of a hemoglobinometer by Loretz with solid state light emitting diode having a wavelength no longer than 553 nm and filter with a cut off of 560 nm, and only relied upon a secondary feature wherein blood turbidity testing can be accomplished by determining and measuring at a wavelength that is near- infrared, i.e. absorbance measurements of blood lipid levels at or near infra-red range which is substantially free from the absorbance of hemoglobin.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the rejection is based on the obvious combination of the teachings of Bradwell with Loretz. To reiterate, Bradwell et al. disclose a nephelometric assay wherein a whole blood sample is lyzed with saponin then reacted with a latex reagent to react with antigens in the whole blood sample to thus, form a reaction mixture, and then

analyzing the reaction mixture. Bradwell et al. achieve to measure the reaction products in the presence of or without the need to remove hemoglobin, by using a second detector to compensate for the amount of light absorbed by the hemoglobin to minimize and correct for any degree of absorption by the hemoglobin in the sample. Loretz is relied upon in combination with Bradwell only for the teaching that blood turbidity, i.e. agglutination, can be determined by measuring at a wavelength that is near- infrared wherein absorbance measurements of analyte, i.e. blood lipid levels, at or near infra-red range are substantially free from the absorbance of hemoglobin. Thus, while both references attempt to achieve the same goal, albeit teaching two different methods to remove any interfering effect by hemoglobin, the choice of a simpler and straight forward method of measurement such as that obtained from the teaching of Loretz is desirable. Further, since Loretz found that absorbance at near infrared wavelength range is substantially free from effects of hemoglobin, one of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the teaching of Loretz, into the method of determining analyte concentration at wavelength range having minimal effect by hemoglobin because by providing a wavelength that totally eliminates unwanted absorbance from interfering substances, hemoglobin, accuracy in assay methods can be better achieved.

B) Applicant argues that Bradwell et al. fail to teach measuring a resultant agglutination mixture for a change in absorbance.

In response, this feature upon which applicant relies (i.e., measuring a resultant agglutination mixture for a change in absorbance) is not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

C) Applicant argues that the combination of Bradwell with Osten does not render obvious the claimed invention. Applicant specifically contends that Osten reference teaches away from the obviousness of 800 nm.

In response to Applicant's argument that Osten reference teaches away from the obviousness of 800 nm, this feature upon which applicant relies (i.e., measuring a resultant agglutination mixture ... which includes a wavelength of 800 nm) is not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). In this case, the rejection is based on the obvious combination of the teachings of Bradwell with Osten. Bradwell et al. is discussed supra. Osten is relied upon in combination with Bradwell only for the teaching that absorbance of matter, i.e. water, in

the near-infrared range of 1150-1190 nm, is substantially free from the absorbance of hemoglobin both in its oxygenated state and deoxygenated state. Thus, while both references attempt to achieve the same goal, albeit teaching two different methods to remove any interfering effect by hemoglobin, the choice of a simpler and straight-forward method of measurement such as that obtained from the teaching of Osten is desirable. Further, since Osten found that absorbance of water in the 1150-1190 nm range is substantially free from the absorbance of hemoglobin both in its oxygenated state and deoxygenated state, one of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the teaching of Osten, into the method of determining analyte concentration at wavelength range having minimal effect by hemoglobin because by providing a wavelength that totally eliminates unwanted absorbance from interfering substances, such as hemoglobin, accuracy in assay methods can be better achieved.

Allowable Subject Matter

8. Claims 15, 19-21, and 23 which recite irradiation and measurement of reaction products at a wavelength range including approximately 800 nm which is substantially free from absorption by both hemoglobin and hemolysis reagent, would be allowable if rewritten or amended to overcome the rejections under 35 U.S.C. 112, second paragraph, set forth in this Office action.

9. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
March 4, 2004

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641